REVIEW ARTICLE

Deep hypothermic circulatory arrest – anesthetic considerations

Hameed Ullah[1]

[1]*Associate Professor, Department of Anesthesiology, Aga Khan University, Karachi (Pakistan)*

Correspondence: Dr Hameed Ullah, Department of Anesthesiology, Aga Khan University Hospital, P O Box 3500, Stadium Road, Karachi – 74800, (Pakistan); Phone: +92 34 86 4637; E-mail: hameed.ullah@aku.edu

ABSTRACT

Deep hypothermic circulatory arrest (DHCA) is the best technique that provides the optimal and bloodless operating conditions as well as brain protection. Although hypothermia is the mainstay of cerebral protection, some pharmacological agents, adequate glucose control, appropriate acid-base management and some surgical techniques that provide selective cerebral perfusion, also help in protecting the brain better and for longer periods of time.

Key words: Deep hypothermic circulatory arrest; Cardiac Surgical Procedures; Heart Arrest, Induced; Induced Hypothermia; Anesthesia

Citation: Ullah H. Deep hypothermic circulatory arrest – anesthetic considerations. Anaesth Pain & Intensive Care. 2016;20 Suppl 1:S115-S118

Received: 16 August 2016; **Reviewed:** 22 August 2016; **Accepted:** 30 August 2016

INTRODUCTION

Deep Hypothermic Circulatory Arrest (DHCA) is, by definition, induction of severe hypothermia (≤ 20° C) during the complete arrest of circulation.[1] The prime objectives are two folds: to provide brain protection by relying upon the protective effects of deep hypothermia on cerebral metabolic rate of oxygen consumption ($CMRO_2$) and a bloodless surgical field so that complex surgery on heart and /or great vessels could be accomplished. DHCA has been used in open-heart surgical procedures where the vessels supplying the head cannot perfuse the brain with standard aortic cannulation and cross clamp. Surgical procedures involving the arch of aorta, great vessels of head and neck and pulmonary vessels benefit from DHCA. It can also be used to reduce the incidence of stroke by preventing the use of cross clamp on aorta with severe atheromas.[2]

PATHOPHYSIOLOGY OF ISCHEMIC BRAIN INJURY DURING DHCA

Ischemic injury to the brain is a serious postoperative concern in patients undergoing DHCA. The pathophysiology of ischemic brain injury is not very well understood, however, reasonable assumptions can be summarized as under. Brain tissue hypoxia causes depletion of adenosine triphosphate (ATP), accumulation of lactate and acidosis leading to cellular dysfunction by failure of Na^+-K^+ ATPase in neuronal cells resulting in cellular swelling and excessive depolarization. This causes excessive release of excitatory neurotransmitters, glutamate and aspartate. Glutamate conversion to glutamine, an energy dependent process, does not happen resulting in its accumulation in neuronal cells causing injury and cell death. Furthermore, lactate production under ischemic conditions causes intracellular acidosis, cell swelling, denaturation of proteins and cell death. Calcium also moves intracellularly forming free-radical peroxidation of lipids. Free-radicals are also formed during reperfusion contributing further to brain cell injury and death. Finally, injury to endothelium releases inflammatory mediators and reduces the production of nitric oxide resulting in increased vascular resistance and worsening tissue hypoxia.

During DHCA, the patient is cooled before arresting cerebral blood flow, and relying on hypothermic reduction of $CMRO_2$. Every degree centigrade of reduction of body temperature reduces $CMRO_2$ by about 6%. Thus at 25° C, $CMRO_2$ is about 37% and at 15° C, $CMRO_2$ is about 15%. Cerebral protective effects of DHCA are multifactorial, hypothermia and

reduced $CMRO_2$ being the most well understood mechanisms. Another factor that may contribute to post DHCA neurological dysfunction is the belief that cerebral autoregulation is disrupted during DHCA causing further ischemia to brain.[3]

SAFE TIME LIMITS

Since the mainstay of brain protection during DHCA is hypothermia, the safe duration of DHCA although controversial, depends upon the patients' body temperature. Reich et al reported a DHCA duration of upto 40 minutes at a body temperature of 12 °C to 15 °C was not associated with neurocognitive decline. Gega et al showed an increased risk of stroke with a DHCA of longer than 40 minutes. Therefore, a safe duration of DHCA would be between 30 – 40 minutes as any duration beyond this is associated with an increased risk of cerebral tissue injury.[4] These limits can be enhanced by using selective cerebral perfusion techniques discussed later.

TEMPERATURE MANAGEMENT

The ideal temperature measurement should reflect core temperature as accurately as possible. Typically there is a difference of 2 °C between cerebral and core and core and peripheral body temperatures respectively. While circulation is intact, various sites can be used for temperature monitoring including jugular venous bulb, urinary bladder, tympanic membrane, nasopharynx, skin and blood from either pulmonary artery catheter or inline temperature probe of cardiopulmonary bypass (CPB) circuit. Although tympanic membrane temperature approximates cerebral temperature, its measurement is difficult during DHCA particularly if external ice is used to cover the head. During DHCA, urinary bladder and nasopharynx can be used reliably.[5]

As cooling is fundamental to DHCA, if not accomplished appropriately, may not provide the intended advantage. As mentioned above, the main beneficial mechanism of cooling is achieved by reducing $CMRO_2$, temperature should be reduced to the range of 15 – 25 °C depending upon the intended duration of DHCA. Time taken to get to these temperatures is extremely important as rapid cooling can lead to cerebral hypoxia by multiple mechanisms. Heterogeneous cooling of brain tissue as blood flow is not uniform for entire brain and although cooled brain is protected, the tissues where adequate temperature is not achieved are still vulnerable to hypoxic injury. As temperature falls, affinity of oxygen for hemoglobin increases, releasing less oxygen to the tissues, aggravating cerebral hypoxia in areas of non-homogenous cooled brain. Cooling, therefore, should be achieved slowly and homogeneously, ideally at a rate of 1 °C every 3 – 5 minutes (slower the better), to avoid the effects of rapid, non-homogeneous cooling of the brain. Means of external cooling should also be employed; particularly by covering head and face (as much as possible) with ice to supplement the principal cooling and also for the prevention of passive rewarming during the duration of DHCA.[6] If electroencephalography (EEG) is being monitored, electrical silence is achieved very late and at temperatures below 15 °C. EEG silence has not been used as a measure of adequate cooling in most centers.

Once the DHCA is reversed, rewarming should also take in a similar time frame as cooling. Once rewarming is complete, the temperatures should be maintained between 35 °C – 37 °C throughout the postoperative period. Postoperative hyperthermia should be avoided as it increases $CMRO_2$, particularly in patients at high risk of cerebral ischemia. Cold reperfusion at 20 °C for 10 – 20 min prior to institution of rewarming has been shown to improve neurological outcome in these patients.[7]

INTRAOPERATIVE MONITORING CONSIDERATIONS

Intraoperative monitoring during procedures requiring DHCA could be divided into routine monitoring for any anesthetized patient, routine monitoring for procedures under CPB and specific monitoring needs for DHCA. Routine anesthetic monitoring should include all standard ASA monitors. For CPB procedures, monitoring should include central venous pressure, invasive arterial pressure, pulmonary artery catheter, cardiac output monitoring whether intermittent or continuous and transesophageal echocardiography (TEE) for hemodynamic management. Blood gas, electrolyte and hemoglobin analysis should also be routinely monitored. Special monitoring considerations for DHCA include bilateral invasive arterial pressure monitoring if antegrade cerebral perfusion is planned.[8] Most important monitoring for DHCA include neurologic monitoring, for which several options exist including somatosensory evoked potentials, EEG, BiSpectral Index (BIS), transcranial Doppler, cerebral blood flow, cerebral oximetry and jugular venous bulb oxygen saturation ($SjVO_2$). All these neurological monitoring modalities

have advantages and disadvantages and varying accuracies, and none of them have shown to reliably predict neurological deterioration during DHCA.

The degree of hypothermia associated with DHCA is known to causes severe coagulopathy. This is further complicated by prolonged CPB time, significant amount of raw surgical area and many suture lines in high pressure vessels. Preoperative arrangement of fresh whole blood, packed red cells, platelets, fresh frozen plasma and cryoprecipitate is essential. Intraoperative use of cell saver and coagulation monitoring should be considered. The use of antifibrinolytic agents to control bleeding may also be useful.[9]

NEUROPROTECTION

During classic DHCA, the entire circulation is arrested including the blood supply to brain and the mainstay of brain protection is hypothermia. In cases where prolonged circulatory arrest is required, selective cerebral perfusion techniques have been developed to reduce the postoperative neurological dysfunction associated with DHCA, In addition there are pharmacological agents that have been used for brain protection during DPB and DHCA.

During selective cerebral perfusion, blood is supplied to the brain either through the venous cannula (retrograde) or through arterial cannulation (antegrade). Normal cerebral blood flow at body temperature during resting condition is around 750 ml/min, which accounts for approximately 15% of cardiac output. During DHCA, the amount of blood flow to the brain is maintained such that adequate and desired hypothermia is maintained. In retrograde selective cerebral perfusion, blood flow to the brain is provided by arterial divergence through the cannula placed in superior vena cava (SVC). Antegrade selective cerebral perfusion uses right axillary artery cannula to perfuse the brain through innominate artery. This route of perfusion depends upon intact and competent Circle of Willis for the perfusion of the left side of the brain. This technique also requires extremely skilled surgeon as this is technically very challenging. Selective cerebral perfusion provides hypothermic blood to the brain maintaining homogenous hypothermia along with oxygen supply to meets the metabolic needs, theoretically providing brain protection. It is also supposed to washout the debris and toxic metabolites, limiting acidosis that may aggravate brain injury thus adding to the prevention of postoperative neurological dysfunction. Disadvantages of selective cerebral perfusion include complication related to cannulation, lack of surgical skill, thromboembolic events and tissue edema of the areas supplied by this circulation including brain.[10,11]

Regarding pharmacological protection, several agents are in use but there is no established practice in this area. Pharmacological agents are used in an attempt to reduce the $CMRO_2$ thus offering neuroprotection. Most commonly used agents for this are barbiturates e.g. thiopentone in high dose and more recently propofol has also been used. Both these agents have shown to produce suppression of brain electrical activity. Inhalational anesthetic agents like isoflurane also provide suppression of EEG but because it does not reduce blood flow to the brain, it cannot be used as a neuroprotective agent. Steroids, dexamethasone and methylprednisolone, are anti-inflammatory and have been shown to offer some brain and spinal cord protection during DHCA, however, their role has not been proven. Some have suggested the use of lignocaine, nicardipine, mannitol, magnesium and etomidate for this purpose.[12]

Adequate glucose management is essential during the entire surgical procedure involving the use of DHCA as hyperglycemia has proven to be associated with worsened neurological outcome. Several factors contribute to intraoperative hyperglycemia. During CPB, there is release of inflammatory mediators causing hyperglycemia and increased insulin resistance. There is also increased secretion of glucagon, growth hormone and catecholamines and reduced levels of insulin, all contributing to hyperglycemia. Insulin administration should be used to maintain a blood glucose concentration below 200 mg/dL. Attention should also be paid to prevent hypoglycemia as it also adversely effects neurological outcome.[13]

ACID–BASE MANAGEMENT (ALPHA STAT AND pH STAT)

There is significant controversy regarding the acid-base management strategy during DHCA. During hypothermia, the solubility of CO_2 increases and pCO_2 decreases and also there is a decrease in dissociation of weak acids and bases in the body which results in alkaline shift of blood pH. Two different strategies are available for acid-base (pH) management. In pH-stat strategy, the pH is managed at the patients' actual temperature and CO_2 is added to maintain a pCO_2 40 mmHg during hypothermia

(temperature corrected). In pH-stat strategy, there is increased cerebral blood flow, probably mediated by increased CO_2 resulting in more homogeneous cooling, greater reduction in oxygen consumption and increased availability of oxygen to the tissues because of left shift of oxyhemoglobin dissociation curve however, this increased cerebral blood flow disrupts the cerebral autoregulation and increases the risk of microembolism to the brain. In alpha-stat strategy, the pCO_2 is allowed to fall depending upon the temperature (non-temperature corrected) resulting in alkaline shift of blood pH. Alpha-stat, on the other hand, preserves cerebral autoregulation i.e. better coupling of cerebral blood flow cerebral metabolism, intracellular pH and enzyme activity. Alpha-stat provides less homogenous cooling and is less efficient.[14] Abdul Aziz in their meta-analysis on this topic concluded that the best technique for acid-base management in patients undergoing DHCA is age dependent with better results using pH-stat in the pediatrics and alpha-stat in the adult patients.[15]

Conflict of interest: None declared by the author.

Author contribution: The author accepts full responsibility for the material presented regarding the concept, the literature search, and manuscript preparation.

REFERENCES

1. Thys DM, Schwartz AJ. Textbook of cardiothoracic anesthesiology: McGraw-Hill, Medical Publishing Division; 2001.
2. Gutsche JT, Ghadimi K, Patel PA, Robinson AR, Lane BJ, Szeto WY, et al. New frontiers in aortic therapy: focus on deep hypothermic circulatory arrest. J Cardiothorac Vasc Anesth. 2014;28(4):1159-63. [PubMed] [Free Full text] doi: 10.1053/j.jvca.2014.03.018.
3. Hensley FA, Martin DE, Gravlee GP. A Practical Approach to cardiac Anesthesia, Fourth Edition. Lippincott, Williams & Wilkins, 2008; 646-648.
4. Gega A, Rizzo JA, Johnson MH, Tranquilli M, Farkas EA, Elefteriades JA. Straight deep hypothermic arrest: experience in 394 patients supports its effectiveness as a sole means of brain preservation. Ann Thorac Surg. 2007;84(3):759-67. [Free Full Text] doi: 10.1016/j.athoracsur.2007.04.107
5. Conolly S, Arrowsmith JE, Klein AA. Deep hypothermic circulatory arrest. Contin Educ Anaesth Crit Care Pain. 2010;10(5):138-142. [Free Full Text] oi: 10.1093/bjaceaccp/mkq024
6. Luehr M, Bachet J, Mohr FW, Etz CD. Modern temperature management in aortic arch surgery: the dilemma of moderate hypothermia, Eur J Cardiothorac Surg. 2014;45(1):27-39. [PubMed] [Free Full text] doi: 10.1093/ejcts/ezt154. Epub 2013 Apr 28.
7. Ziganshin BA, Elefteriades JA. Deep hypothermic circulatory arrest. Ann Cardiothorac Surg 2013;2(3):303-315. [PubMed] [Free Full text] doi: 10.3978/j.issn.2225-319X.2013.01.05.
8. Svyatets M, Tolani K, Zhang M, Tulman G, Charchaflieh J. Perioperative Management of Deep Hypothermic Circulatory Arrest. J Cardiothorac Vasc Anesth 2010; 24(4):644-655. [PubMed] [Free Full text] doi: 10.1053/j.jvca.2010.02.010. Epub 2010 May 15.
9. Reed H, Berg KB, Janelle GM. Aortic Surgery and Deep-Hypothermic Circulatory Arrest: Anesthetic Update. Semin Cardiothorac Vasc Anesth. 2014 Jun;18(2):137-45. [PubMed] [Free Full text] doi: 10.1177/1089253214525278.
10. Chau KH, Ziganshin BA, Elefteriades JA. Deep hypothermic circulatory arrest: real-life suspended animation. Prog Cardiovasc Dis.. 2013;56(1):81-91. [PubMed] [Free Full text] doi: 10.1016/j.pcad.2013.05.009.
11. Reich DL, Uysal S, Sliwinski M, Ergin MA, Kahn RA, Konstadt SN, et al. Neuropsychologic outcome after deep hypothermic circulatory arrest in adults. The Journal of thoracic and cardiovascular surgery. 1999;117(1):156-63. [PubMed] [Free Full text] doi: 10.1016/S0022-5223(99)70481-2
12. Al-Hashimi S, Zaman M, Waterworth P, Bilal H. Does the use of thiopental provide added cerebral protection during deep hypothermic circulatory arrest? Interact Cardiovasc Thorac Surg. 2013;17(2):392-7. [PubMed] [Free Full text] doi: 10.1093/icvts/ivt184.
13. Shine TS, Uchikado M, Crawford CC, Murray MJ. Importance of perioperative blood glucose management in cardiac surgical patients. Asian Cardiovascular and Thoracic Annals. 2007;15(6):534-8. [PubMed] [Free Full text] doi: 10.1177/021849230701500621
14. Duebener LF, Hagino I, Sakamoto T, Mime LB, Stamm C, Zurakowski D, et al. Effects of pH management during deep hypothermic bypass on cerebral microcirculation: alpha-stat versus pH-stat. Circulation. 2002;106(12 suppl 1):I-103-I-8. [PubMed] [Free Full text] doi: 10.1161/01.cir.0000032916.33237.a9
15. Aziz KAA, Meduoye A. Is pH-stat or alpha-stat the best technique to follow in patients undergoing deep hypothermic circulatory arrest? Interact Cardiovasc Thorac Surg. 2010;10(2):271-82. [Free Full Text] doi: 10.1510/icvts.2009.214130

★★★★★